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NOTE

The Next Course in the Medical Aspects of Special Weapons and Radioactive Isotopes for U. S. Naval Reserve Medical and Dental Officers at the U. S. Naval Medical School, National Naval Medical Center, Bethesda, Maryland:

27-31 March 1950

Effect of Choline as a Lipotropic Agent for Treatment in Coronary Atherosclerosis: It is becoming more evident that lipotropic agents such as choline, a member of the vitamin B complex, are effective in the prevention of experimental and clinical fatty infiltration and degeneration of the liver, and in experimentally induced atherosclerosis. Because numerous observers have described data from which it was concluded that a disorder in lipoid or cholesterol metabolism is a significant factor in the development of human atherosclerosis and because of the encouraging lipotropic action of choline on atherosclerosis in experimental animals, the authors carried out a study over a 3-year period on the lipotropic action of choline in 230 patients with proven coronary artery atherosclerosis. These patients were admitted in consecutive order to the Los Angeles County General Hospital medical wards. One hundred and fifteen of the patients served as controls; these were discharged from the hospital on recovery after an average period of 6 weeks and were then followed over a 3-year period. They were not given choline; some were given whatever medication may have been indicated for symptoms; in patients who were symptom-free no medication was prescribed but their progress was ascertained periodically. The other group of 115 patients represented those who were admitted to the hospital in alternate order for their first acute myocardial infarction. After they were discharged from the hospital, they were placed on choline treatment over a 3-year period and followed in the research clinic of the hospital. Fifty-two patients were given choline for one year, 35 patients took choline for 2 years, and 28 patients were given choline for 3 years. The dosage of choline varied from 6 to 32 Gm. daily, depending on the tolerance for the drug and the degree of hypercholesterolemia present. Choline bicarbonate was used in this study. The diet remained the same as that taken by the patients prior to their infarction; patients with their first known infarction only were studied. The ages for the controls ranged from 30 to 70 years, and for the choline-treated patients, from 28 to 70 years; most patients were of the white race and were males.

Of the 115 control patients, 35 (30 percent) had died after 3 years. Death in this series resulted from recurrent coronary thrombosis with myocardial infarction (19 cases), congestive heart failure (10 cases), or extracardiac causes (6 cases). In the choline-treated series of 115 patients, 14 (12 percent) had died after 3 years; death resulted from recurrent coronary thrombosis with myocardial infarction (6 cases), congestive heart (5 cases), or to extracardiac causes (3 cases). The mortality rate mainly from cardiac cause in the control series was 30 percent as against 12 percent for the choline-treated patients.

Previous clinical and experimental observations on the action of choline in preventing or mitigating experimental atherosclerosis have suggested that this lipotropic agent like that of its fellow members of the vitamin B complex, inositol, pyridoxine, and methionine, appears to prevent arterial atheromatous deposition or to exert a decholesterolizing effect on the atheromatous deposits in the vascular walls of experimental animals, and in man. (Proc. Soc. Exper. Biol. and Med., Jan. '50, L. M. Morrison and W. F. Gonzales)

Reduced Absorption of Aureomycin Caused by Aluminum Hydroxide Gel (Amphojel): It has been recommended that aureomycin be prescribed along with a preparation of aluminum hydroxide suspension which will in some instances reduce the epigastric distress, nausea, and vomiting that occasionally occur when aureomycin is given alone. However, it has been found that solutions of aureomycin have very little antibacterial activity following exposure to aluminum hydroxide gel. This observation suggested that if aluminum hydroxide is administered concurrently with aureomycin, similar loss of activity might occur in the bowel and greatly diminish the anticipated levels of the drug in the blood and tissues. The present report is therefore concerned with the influence of an orally administered aluminum hydroxide suspension upon the absorption of aureomycin as measured by aureomycin blood levels obtained before and after aluminum hydroxide was instituted.

Daily levels of aureomycin in the serum of 5 hospitalized patients and 6 normal male subjects were determined. Aureomycin was administered for 3 consecutive days. This was followed immediately by a 3-day period during which aureomycin and aluminum hydroxide suspension were both administered. The dose of aureomycin was 500 mg. taken orally every 6 hours. Two tablespoons of aluminum hydroxide gel were given immediately after each dose of aureomycin.

In 4 patients, there was a fall in the level of aureomycin in the serum within 24 hours after beginning the aluminum hydroxide gel with aureomycin. After 48 hours of the combined medication, all serum levels were less than 1 mg. per ml. Aureomycin without amphojel produced levels which averaged 5.9 mg. per ml. in spite of the aluminum hydroxide. One patient suffered a recurrence of her urinary tract infection on the third day of combined treatment which promptly subsided when the aluminum hydroxide was discontinued. In each of the 6 normal males, the addition of aluminum hydroxide gel was followed within 24 hours by a sharp drop in the serum concentration of aureomycin. Levels before aluminum hydroxide gel averaged 4.2 mg. per ml. and ranged from 1.25 mg. per ml. to 10.24 mg. per ml. After aluminum hydroxide gel, the average level was 0.49 mg. per ml. with a range of from 0.036 mg. per ml. to 1.25 mg. per ml. Four of the normal male subjects complained of loose unformed stools during the 6 days they were taking aureomycin. Three of them noted anal pruritus that disappeared after aureomycin was discontinued.

This lowering of the serum level of aureomycin by aluminum hydroxide gel may explain some therapeutic failures in infections in which there is usually a response to aureomycin. Aluminum hydroxide gel and aureomycin should not be used together. (Proc. Soc. Exper. Biol. and Med., Jan. '50, B. A. Waisbren and J. S. Hueckel)

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Preliminary Observations on the Antiarthritic Effect of 21-Acetoxypregnenolone: It has been shown by Seifter et al, that the permeability of the synovial membrane in rabbits is influenced by enzymes and by steroids. Hyaluronidase and desoxycorticosterone were found markedly to increase permeability; cortisone was the most effective in inhibiting permeability through normal and through hyaluronidase-treated membranes. The alarm reaction and the administration of adrenocorticotropic hormone were as effective as cortisone. These data were interpreted to mean that normal permeability of the synovial membrane is maintained by a balance between the opposing actions of the 2 types of adrenal steroids on the ground substance mucopolysaccharides such as hyaluronic acid. According to this view bacterial infection with release of enzymes such as hyaluronidase, or adaptation disease characterized by excess production of desoxycorticosterone, depolymerize the mucopolysaccharides of the ground substance and permit the formation of edema and swelling of the membrane. Cortisone alters the mucopolysaccharides so that they become more resistant to enzymes and desoxycorticosterone, their water binding capacity is decreased, and they become freed from edema.

Seifter et al, considered the therapeutic effect of cortisone in arthritis to consist of at least 3 phases: (1) immediate antienzyme or antidesoxycorticosterone effect on the synovial membrane (end organ) resulting in alleviation of edema and swelling; (2) healing action on synoviae possibly by general effects on carbohydrate metabolism; and (3) general metabolic effect on the rheumatoid state. They employed the rabbit synovial membrane technic to screen more than 20 steroids and to compare their efficiency with cortisone on the end organ. The barrier effect of cortisone was rated as 100 percent. All but 2 of the steroids screened decreased permeability of the synovial membrane. Pregnenolone, testosterone, combinations of these, and most of the other steroids had less than 40 percent cortisone effect. Two steroids were found to be at least as active as cortisone. One of these, 21-acetoxypregnenolone, had activity 130 percent that of cortisone. It also antagonized the effect of desoxycorticosterone and hyaluronidase on the synovial membrane. The antidesoxycorticosterone effect was 5 times as great as the antihyaluronidase effect. Comparison of the formula of this compound with that of desoxycorticosterone indicated resemblance of structure sufficient to warrant consideration of its action as a competitive inhibitor of desoxycorticosterone.

The authors decided to employ 21-acetoxypregnenolone as an investigative tool to determine whether the simple end organ effect would be sufficient to alleviate rheumatoid arthritis or whether the other actions of cortisone contribute an important role in the treatment in this disease. In this paper are reported the preliminary observations which confirm the findings in the rabbit studies. Evaluation of 21-acetoxypregnenolone as a treatment is being carried out on a separate group of hospitalized patients on whom the customary laboratory investigations of the rheumatoid state and necessary metabolic studies are being made.

Seven patients were selected for this preliminary study according to the following criteria: (1) the patient must have rheumatoid arthritis of a moderate or marked degree, (2) the rheumatic process must be demonstrably active, and (3) the patient must be ambulatory and engaged in his usual activity. One patient, case no. 7, was hospitalized and placed at bed rest. Ambulant cases were selected in an attempt to minimize the known beneficial effects of bed rest. All patients had previously received routine arthritic management. With the exception of case no. 6, each patient was given 100 mg. cholesterol daily by intramuscular injection for 3 days prior to the administration of 21-acetoxypregnenolone. Twenty-one-acetoxypregnenolone was then administered intramuscularly, 100 mg. the first day, 200 mg. the second day, and 300 mg. daily thereafter for a total period of 14 days. At the end of this period the dosage was decreased to 200 mg., and the interval was lengthened to 2 days. Each patient was examined daily by one of the authors and at 3-day intervals by all of the authors. Improvement in over-all function, swelling, pain, local inflammation, and joint tenderness was measured in accordance with the Criteria for Gauging Rheumatic Improvement as agreed upon by the New York Rheumatism Association: grade O = no improvement; grade + = slight; grade ++ = moderate; grade +++ = marked; grade ++++ = very marked.

Case no. 1. M. H., 39 years old, a typist, had had rheumatoid arthritis for 2 and 1/2 years. The joints chiefly involved were both shoulders and interphalangeal joints of both hands. No change in subjective or objective findings was noted during 3 days of cholesterol administration. Significant improvement was first noted on the fourth day of 21-acetoxypregnenolone administration. Grade +++ improvement in pain, tenderness, and function was noted by all observers on the fifth day. Improvement continued over a period of 2 weeks, and the patient stated that typing had greatly improved, fatigue had lessened, and sense of well being had improved; improvement was rated as grade ++++. Slight return of swelling and tenderness accompanied reduction of dosage and lengthening of interval. A weight gain of 2 lbs. in 2 weeks was noted with no evidence of fluid retention.

Case no. 2. H. B., a 34-year-old housewife, had had rheumatoid arthritis for 16 years. The joints chiefly involved were both knees, left elbow, and right wrist. The patient reported an aggravation of symptoms during 3 days of cholesterol therapy. Significant improvement was first noted on the third day of 21-acetoxypregnenolone administration. Improvement in euphoria, function, pain, tenderness, and swelling was rated as grade +++ on the fifth day. Improvement over a period of 2 weeks was rated as grade ++++ and the patient was able to climb stairs for the first time in 2 years. Reduction in dosage and lengthening of interval did not cause regression in symptoms. The patient gained 1 and 1/2 lbs. in a period of 2 weeks and showed no evidence of fluid retention.

Case no. 3. N. N., a 56-year-old housewife had had rheumatoid arthritis for 5 years. The joints chiefly involved were the left wrist and left knee. The patient reported aggravation of symptoms during 3 days of administration of cholesterol. Significant improvement was noted on the third day of 21-acetoxypregnenolone administration. Evaluation on the fifth day revealed remarkable reduction in swelling and grade +++ improvement in local inflammation, tenderness, pain, function, and general mood. By the eighth day the patient reported that she had no arthritic symptoms. Evaluation of improvement at the end of a period of 2 weeks revealed grade ++++ improvement in all phases. Reduction in dosage and lengthening of interval was attended by only a slight regression in the previously noted improvement. The patient had a total weight gain of 1 lb. in 2 weeks and showed no evidence of fluid retention.

Case no. 4. A. S., a 43-year-old housewife had had rheumatoid arthritis for 8 years. The joints chiefly involved were both shoulders, right wrist, right elbow, and metacarpophalangeal joints. This patient was in a severe relapse at the start of treatment and was becoming rapidly worse. Three days of cholesterol therapy seemed to aggravate her symptoms. The first significant improvement was noted on the eighth day of treatment with 21-acetoxypregnenolone. Evaluation at the end of a period of 2 weeks was rated as grade +++ improvement in general function and in all joints. Reduction in dose and lengthening of interval resulted in a moderate relapse in the previously noted improvement. The patient gained no weight during an interval of 2 weeks, and there was no evidence of fluid retention.

The histories as recorded by the authors for the other 3 patients are essentially the same as the four above. (Proc. Soc. Exper. Biol. and Med., Jan. '50, J. Seifter et al.)

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The Huggins Cancer Test on 700 Normal Persons: Huggins et al. have demonstrated that blood serum from persons with cancer, when heated at 100° C. for 30 minutes, coagulates less readily than does normal serum. This defect in serum from persons with cancer can be accurately detected by the use of an inhibitor to coagulation, sodium iodoacetate, at a pH of 7.4. To permit mathematical expression of this phenomenon, Huggins proposed the iodoacetate index, which would be obtained by dividing the number of micro-moles of iodoacetate required to inhibit coagulation of one milliliter of serum by the number representing the total protein of the serum in grams percent. In a group of 283 individuals (100 normals, 88 cancer patients, and 95 patients with nonmalignant pathology), 85 patients with clinically active cancers had indices of less than 9.0, as did 16 patients with nonmalignant pathology. All normals fell within the range of from 9.2 to 12.6. Because it is equally important to know how often one may expect an index below 9.0 in healthy persons, the authors have determined the iodoacetate index of 700 apparently healthy men and women of various ages at a large Army training center.

In this survey, the method, reagents, and equipment to determine the iodoacetate index were exactly the same as those used by Huggins and his co-workers. The age range of the individuals studied was from 17 to 56 years. Seventy-five percent were below age 24. Twenty-five sera of cancer patients were obtained and used as controls in the performance of the thermal coagulation tests on the normal sera.

Of the 700 individuals tested, the iodoacetate index of all fell within the range of from 9.3 to 13.7. The mean value was 11.27. The median was 11.10. Neither age nor sex significantly influenced the iodoacetate index. In 6 instances, the original determination yielded values of less than 9.3, ranging from 7.78 to 9.08. However, repetition of these determinations yielded normal values in each case, the results ranging from 9.76 to 12.18. Of the 25 sera from cancer patients used for controls, 6 gave values higher than 9.3, ranging from 9.38 to 11.96. The remaining 19 values ranged from 3.06 to 8.95. Only those sera yielding an iodoacetate index of less than 9.0 were used as control sera in the survey. Of the 6 patients within the control group presumed to have cancer and who gave values within the normal range, from 9.38 to 11.96, one was later determined to have a benign gastric polyp, and one was diagnosed as lymphosarcoma but had been receiving extensive x-ray therapy. The results in the 4 remaining cases are not explained. Their respective diagnoses are leukemia, adenocarcinoma of the rectum, carcinoma of the mandible, and generalized metastatic carcinoma, primary site unknown. One patient thought to have cancer of the uterine cervix gave an iodoacetate index of 4.24; however, a diagnostic curettage did not reveal malignant cells.

It appears that the iodoacetate index is uniformly negative in normal individuals. The technic is relatively simple and within the scope of the laboratory technician qualified to use an analytical balance in the preparation of the necessary reagents. The thermal coagulation endpoint is striking and quite reproducible. All determinations yielding abnormal indices should be repeated. In no instance of multiple determinations upon the same serum specimen have the results varied more than one tube. In general, the authors' findings on the sera of cancer patients coincide with those of Huggins. (Proc. Soc. Exper. Biol. and Med., Jan. '50, L. Kiefer et al.)

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Clinical Experience with Thiomerin: Various sulfhydryl-containing substances have been shown to diminish the toxicity of mercurial diuretics without necessarily impairing their diuretic action. One such combination which appears to have excellent diuretic properties is thiomerin. This is identical with mercuzanthin except that the theophylline link is replaced by sodium mercaptoacetate. The drug is readily soluble in water, and can be given subcutaneously.

The purpose of this report is to recount the clinical experience with thiomerin in 205 patients treated on the wards and in the cardiac clinic of the Gouverneur Hospital, New York City.

In the 11-month period from May 1948,to April 1949, 3,314 injections totalling 5161.5 cc. of thiomerin were given. One hundred and seventy-three patients had heart disease, the majority being of hypertensive or arteriosclerotic origin. All had the usual systemic or pulmonary manifestations of heart failure in varying degrees. Of the 32 patients who had no heart disease, 11 had portal cirrhosis of the liver with ascites; 3, carcinomatosis with ascites; 2, chronic glomerulonephritis; one, mesothelioma of the peritoneum; one, postfilarial elephantiasis; and 14, miscellaneous diseases without edema. The non-edematous patients were part of the control group.

The distribution according to number of injections of the drug was as follows: from 55 to 135 injections, 20 patients; from 25 to 50 injections, 21 patients; from 10 to 24 injections, 34 patients; from 3 to 9 injections, 52 patients; and from one to 2 injections, 78 patients.

The drug was injected subcutaneously in every case, except for 14 intravenous trials. Injections were made into the upper parts of the arms. Thiomerin was used in the same dosage and with the same frequency as the common mercurial diuretics. In the first few weeks it was given to several patients who had been under treatment with mercuhydrin, but later it was used as the sole diuretic. Management was otherwise unchanged; bed rest, digitalis, dietary restriction, and other measures were applied as indicated. No ammonium chloride or other acidifying salts were used. Five patients, whose cooperation and intelligence were assured, were permitted to receive most of their injections at home. Only one administered the drug himself. The other 4 received it from members of the family.

In urine output measurements which were made on 30 patients, unequivocal diuresis occurred in all but one of the trials. The mean 24-hour outputs before and after thiomerin were as follows: control, 1110 cc.: after 1 cc. subcutaneously, 1913 cc. (24 cases); control, 1369 cc.: after 1 cc. intravenously, 2203 cc. (4 cases); control, 1121 cc.: after 2 cc. subcutaneously, 2870 cc. (18 cases); control 1177 cc.: after 2 cc. intravenously, 2576 cc. (10 cases). The time of onset of diuresis varied from the end of the first hour to the end of the fifth hour after 1 cc. subcutaneously; from the end of the first to the end of the fourth hour after 2 cc. subcutaneously, and from the end of the first to the end of the third hour after 2 cc. intravenously. The peak of diuresis followed a roughly similar distribution, but occurred about one hour later.

The patients with congestive heart failure responded to the drug in an entirely satisfactory manner. In those cases in which another mercurial diuretic had been used just before thiomerin was started, the latter drug appeared to be at least as effective. In 12 cases, there was greater diuresis after thiomerin than after mercuhydrin in similar doses, but this was not taken as indication of greater efficacy of the newer drug because of the complexity of other factors such as the effect of bed rest, diet, and digitalization.

Five patients with intractable congestive failure, all of whom died, failed to respond to repeated injections of thiomerin. In a case of peritoneal mesothelioma there was similar failure of response.

Most of the patients with ascites and edema as a result of hepatic cirrhosis showed from fair to moderate diuresis after thiomerin. In one case of chronic glomerulonephritis there was striking diuresis. In the case of post-filarial elephantiasis, which was of 30 years' duration, thiomerin was very effective, although the edema reaccumulated rapidly.

No instance of a general toxic reaction was noted, nor was there a single case of hypersensitivity of the usual type with the common allergic manifestations. Reactions attributable to excessive electrolyte or water loss did not occur or were so mild as to be missed. Spontaneous re-digitalization consequent upon diuresis was not detected.

Local reactions occurred in 8 patients. These usually consisted of subcutaneous nodules, often tender, and sometimes preceded by hematomas. The nodules varied in size from 3 to 20 mm. They appeared in from 2 to 4 days after injection and completely disappeared within 4 weeks, except for one case in which 2 nodules were present after 5 months. Ecchymoses or hematomas not followed by nodules were observed in a few cases. The local reaction was severe in only one patient, a 49-year-old woman with rheumatic heart disease. After her sixteenth injection of 2 cc. of thiomerin, an ecchymosis appeared in the right deltoid region. This became indurated and sloughed in 9 days, leaving a clean ulcer about 1.5 cm. across which healed well. Subsequent to the appearance of the ecchymosis, she received 3 more injections in the next 8 days without untoward event. It was considered probable that her reaction resulted from inadvertent intracutaneous administration or possibly secondary infection. Six of the 8 patients with local reactions were obese women, with considerable adiposity of the arms. In one case, after a nodule had developed in each arm, one injection was made into the subcutaneous tissue of the dorsum of the hand with no subsequent local reaction.

It is of interest that the nodules appeared during the first 6 months of this study. None was noted after November 1948. Information from the manufacturer reveals that the earlier batches of the drug contained from 2.5 to 3 percent moisture, which resulted in a tendency for the powder to decompose on standing at room temperature. Subsequently this was corrected, and the currently made product has less moisture content and more stability. Incidentally, in none of 5 patients who received most of their thiomerin at home, administered by themselves or for them by a member of their family, did any local reaction occur. These patients received almost 300 injections in their homes.

Autopsies were obtained on the bodies of 5 patients who had received 3 or more doses of thiomerin. Two had received 3 injections; one, 4; one, 13; and one, 18. In no instance was there any gross or microscopic evidence suggestive of mercurial poisoning. Tubular lesions were found in one case.

Experience with this new drug is too little to indicate with certainty that general toxic effects will be less frequent than with the commonly used mercurials. The latter, even by the intramuscular route, have been implicated in nephrotoxic reactions. Since thiomerin intravenously has been shown to possess only a small fraction of the cardiac toxicity of the other preparations, it is to be expected that the incidence of general toxic reactions will be less. In the authors' case of nephritis and nephrosis there was no indication that death was caused by thiomerin. It is conceivable, however, that the tubular lesions may have been aggravated by the mercurial.

A safe and efficient mercurial diuretic that can be injected subcutaneously by the patient himself or for him by a member of his family will result in a considerable saving of expense and physical effort for the patient. (The thiomerin used in this study was supplied by Campbell Products, Inc., New York City.) (Am. J. M. Sc., Feb. '50, C. D. Enselberg and H. G. Simmons)

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Rheumatic Fever in the Navy in the Postwar Period: Rheumatic fever in the Navy and Marine Corps during World War II was discussed in the February 1950 issue of Statistics of Navy Medicine (Navy Medical News Letter of 10 February 1950).

For the postwar 3-year period, 1946-1948, there were 5,074 cases of rheumatic fever reported among Navy and Marine Corps personnel. There were also 208 readmissions for this condition, or one readmission for each 24 new cases. These 5,074 cases represent 7.7 percent of the total of class XIII (Other Diseases of the Infectious Type). However, they contributed a total of 837,822 sick days, accounting for almost 60 percent of the sick days for all of class XIII. This means that there was an average of 764 individuals on the sick list throughout the 3-year period with rheumatic fever. This figure is weighted somewhat by the fact that more than half of the disease incidence and sick days was ascribed to the single year, 1946. Even in 1948 there were on the average 30 men out of every 100,000 average strength noneffective because of this diagnosis. The noneffective rate decreased from 1.3 in 1946 to 0.3 in 1948. Inasmuch as a reduced noneffective rate is the reflection of a decrease in the incidence rate or in the length of stay of individuals on the sick list (or both), the degree to which they contribute to this reduction may be observed. The reduction in the incidence rate of 65 percent from 1946 to 1948 had somewhat greater weight than did the 26 percent reduction in the average number of sick days per new case. The average number of sick days in 1946 was 167.6 which increased to 181.3 days per case in 1947 and was followed by a reduction to 123.7 days in 1948.

The shrap drop in the incidence rate for this condition from 2.9 per 1000 strength in 1946 to 1.2 in 1947 probably reflects to some degree those

cases revealed through physical examinations during the peak period of separations from the service in 1946. There has been little significant change in the incidence rate during the subsequent years, the rate remaining at approximately 1 per 1000 average strength, which is half of the average rate for rheumatic fever during the war years.

Of major importance are the complications or sequelae of rheumatic fever, the most frequently occurring of which are valvular heart conditions. This involvement was found in one out of every 6 cases of rheumatic fever. The distribution also shows that mitral insufficiency occurred in well over 50 percent of the cases in which complications or sequelae were reported. In only 7 percent of the cases in which there were complications or sequelae were there conditions other than some form of valvular heart disease.

Invaliding from the service (IS) as a result of rheumatic fever during the 3-year period 1946-1948 shows that for every 100 patients with new cases diagnosed, 32 were given medical discharges for this condition; in 1946 there were 1,416, representing a rate of 370.1 per 1000 new cases; in 1947, there were 151, representing a rate of 206.3 per 1000 new cases; and in 1948 there were 49, representing a rate of 95.0 per 1000 new cases.

It is very probable that many patients who had rheumatic fever were subsequently invalided from the service for some other condition, such as valvular heart disease. (Statistics of Navy Medicine, March 1950)

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Minimum Requirements for Effective Machine Dishwashing: To make it possible for Federal agencies to take advantage of the latest knowledge in making new installations of dishwashing machines the Committee on Sanitary Engineering and Environment, Division of Medical Sciences, National Research Council, through its Subcommittee on Food Supply, developed and presents below, Recommended Minimum Requirements for Machine Dishwashing. The general adoption of these minimum standards would simplify for all users the problem of procuring the types of dishwashing machines and auxiliary equipment required for dishwashing and installations that can be operated with consistently good results.

It is not anticipated that these standards will be applied to existing installations of dishwashing machines. The remodeling of an old machine to meet a single item of the minimum requirements may accomplish nothing. Among the few items that may be singled out to improve efficiency is that of prerinsing the dishes. Otherwise full compliance with all details of these requirements is essential to make old installations operate efficiently. In general, it is likely to be cheaper to install new equipment meeting the requirements than to overhaul old installations.

Recommended Minimum Requirements for Machine Dishwashing

(Revised - 14 February 1950)

Status. This is a tentative functional specification designed to incorporate the results of recent studies of the efficiency of mechanical dishwashers.

Objective. To treat soiled eating and drinking utensils so as to remove all visible soil, wash water, and detergent, leave them clean and reasonably dry, and effectively reduce the public health hazard.

Scraping. Food remains shall be removed from the dishes by hand or suitable mechanical device.

Preflushing. The preflushing of dishes with warm water, with or without detergent, is highly desirable. This may be done in a preflush section of the dishwashing machine of demonstrated effectiveness or as a separate operation. The warm water containing detergent overflowing from the wash water tank or overflow rinse water may well be utilized for preflushing.

Racks and Racking. The dish racks shall be of such design as to minimize masking of the sprays. Construction with nonmarking corrosion-resistant welded wire is recommended. The number of each type of utensil per rack shall be limited as overcrowding prevents effective washing. A sufficient number of racks shall be provided to permit continuous operation under maximum load. Means shall be provided for returning empty racks without damage or contamination from the outlet to the inlet end of the machine.

Washing. The temperature of the wash water shall be not less than 140° F. With good preflushing, higher temperatures, i. e., 160° F. or more are desirable. Means shall be provided to maintain the temperature of the wash water at not less than 140° F. The minimum time of washing shall be 20 seconds, during which time each rack of dishes shall be sprayed from above and below in about equal amounts with a total of not less than 12 gallons of wash water per 100 square inches of tray area under not less than three pounds flow pressure at the top manifold. In single tank machines the time of washing shall be controlled automatically at not less than 40 seconds and in multiple tank machines such time shall be controlled at not less than 20 seconds by timed conveyors with effective method to prevent racks from being pushed through. Means should be provided to maintain the concentration of detergent in the wash water automatically and continuously at not less than 0.1 percent by weight in excess of that necessary to satisfy the hardness of the water. In multiple-tank dishwashing machines excessive spilling or carry-over of water shall be prevented by providing at least 15 inches of space between the beginning of the wash tank and the center of the first spray arm opening, at least 20 inches between the centers of the last wash spray arm opening and the first rinse spray arm opening, at least 5 inches between the center of the last rinse spray arm opening and the curtain rinse opening, and not less than 10 inches between the center of the last curtain rinse spray opening and the end of the rinse tank. When necessary, because of extended spray patterns or otherwise, baffles shall be installed between the wash and rinse tanks to prevent further intermingling of wash and rinse waters.

Rinse. A power or recirculated rinse (two-tank machine) is desirable wherever the quantity of utensils to be washed justifies the cost and the space available for installation permits. The temperature of such rinse water shall be not less than 180° F. at the inlet to the spray arm. The minimum time of rinsing shall be 10 seconds, during which time each rack of dishes shall be sprayed from above and below in about equal amounts with a total of not less than 12 gallons of rinse water per 100 square inches of area under not less than 3 pounds flow pressure at the nozzles. Where this rinse is used as the sanitizing rinse provision shall be made to stop the machine automatically and to display a warning light whenever the temperature of the rinse water drops below 180° F. A key-operated device shall be provided to permit starting and operating the machine in emergencies at less than the recommended temperature. When a recirculated rinse is not provided, as in single-tank machines, the fresh water rinse from the pressure line shall be maintained at a temperature of not less than 180° F. at the inlet to the spray arm and provided with automatic stop and warning

light as above. The minimum time of rinsing shall be 10 seconds during which time each rack of dishes shall be sprayed with not less than 3/8 gallons of fresh water per 100 square inches of area under not less than 15 pounds flow pressure at the nozzles. Provision shall be made to stop the machine automatically and to display a warning light whenever the temperature of this rinse water drops below 180° F. A key-operated device shall also be provided for emergency operation.

Curtain Rinse. A curtain rinse is not required. A top limit of two gallons of water per minute is proposed for such a rinse, if provided, in order to limit this ineffective use of hot water.

Removal of Vapors. Where excessive moisture accumulates and causes condensation, the installation should include suitable means for ventilation and removal of the excess vapor.

Valves. The water and steam valves shall be of dependable construction, easily accessible, marked with standard designating colors in accordance with A.S.A.: A 13-1928 "Scheme for the Identification of Piping System," labeled as to purpose, and shall not so protrude as to be easily broken off. Valves shall be suitable for the purpose and built to withstand 125 pounds operating pressure. The water valves shall be of globe type with removable seats.

Thermometers. A dial-type thermometer with 180° F. visibly marked, showing final rinse water temperature, shall be installed at eye level near the discharge end of the machine where it is protected against breakage. The bulb shall be located so as to show the temperature of rinse water entering the spray arm. Similarly, a thermometer shall be installed to show the wash water temperature.

Pressure Gages. Gages shall be provided to show the flow pressure as near as practical to the spray arm openings of both the wash and rinse water systems.

Scrap Trays. Scrap trays shall have openings smaller than those in the spray arm and shall be readily accessible and removable for cleaning. A strainer, accessible for cleaning, shall also be provided on the pump suction.

Spray Arms. Spray arms shall be made of material that is relatively noncorrodible in warm detergent solution and shall be easily removable and accessible for cleaning. The slots or jet openings shall be large enough not to clog easily and shall be so placed as to completely spray every part of every utensil in racks of the standard size delivered with the machine. Either the spray arms shall move or the dish racks shall be moved during washing and rinsing to increase the coverage of the sprays.

Construction. The tanks and hood shall be constructed of monel metal, stainless steel or equally corrosion-resistant material in such a manner as to be easily cleaned. Sharp angles, unnecessary ledges, and open seams shall be eliminated. To facilitate cleaning of the interior, consideration should be given to locating as much of the piping as possible on the exterior of the dishwashing machine. Each tank including the pump, shall be easy to drain. The pump suction shall be at least two inches above the bottom of the tank. Each tank shall be provided with a water level indicator. The supporting frame, motors, and pumps shall be of smooth construction with all parts accessible for cleaning. Adequate guards shall be placed over moving parts. The bottom platform of the machine shall be not less than six inches off the floor. Side clean-out doors or removable panels not less than 16 inches in width shall be provided for convenience in cleaning the tanks. All valves, fittings, and pipes shall be so placed as to avoid obstructing door openings. Conveyors shall be so timed that the fixed speed will provide at least the minimum holding times herein specified for the various operations.

Water Supply. Water meters that are too small and water mains that are too small or too badly encrusted to deliver sufficient water for the sanitizing rinse under the existing conditions of

installation are a frequent cause of failure of dishwashing operations. When the hardness of the water exceeds five grains per gallon (85.5 ppm) a hard water detergent should be used; when it exceeds 10 grains (171 ppm), softening to five grains or less is recommended. In order to secure uniform water pressure the installation of a pressure-reducing valve on the hot water line to the fresh water rinse of the dishwashing machine is recommended, so set as to give 15 pounds flow pressure at the upper rinse arm openings while in operation. The water connections to the dishwashing machines shall be so made as to prevent back-siphonage of dish water, sewage or wastes, and in accordance with A.S.A.: A 40.6-1943, "Back-flow Preventers." The hot water storage tank shall be of ample capacity and the heater shall have sufficient recovery capacity to supply the amount of water, at not less than 140° F., needed for maximum length dishwashing periods and other operations for which it is designed to provide water, if carried on simultaneously. Means shall be provided, as by booster heater with or without storage tank, to supply not less than 2 and 1/4 gallons per 100 square inches of tray area per minute of water at 180° F. or higher at the inlet to the spray arms for single tank machines, and as much as two gallons per minute of water at 180° F. for each curtain rinse on a multiple tank machine. Adequate provisions shall be made to prevent the delivery of water at less than 180° F. at the spray arms when operation starts after the machine has stood idle for one hour.

Sewer Connection. There shall be an airbreak in the line carrying drainage and overflow from the machine to the sewer to prevent possible backflow of sewage into the machine.

Placing. The machine shall be so installed that all parts are easily accessible for repair, servicing, or replacement.

Operating Instructions. Complete operating instructions shall be provided. Such instructions shall stress draining the tanks empty after the dishes from each meal are finished, cleaning the tanks and spray arms, and leaving them dry until the next use. (NRC report dated 14 February 1950)

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Treatment in Leprosy with Diamino-Diphenyl Sulfone by Mouth: Diaminodiphenyl sulfone (DADPS) was the first sulfone synthesized (1908) but its pharmacology and its therapeutic effects were not studied until 1937, when Buttle et al. found that it possessed remarkable properties. In streptococcal infections in mice, doses of 0.4 mg. were as effective as doses of sulfanilamide a hundred times greater; and doses of 0.04 mg. were only slightly less effective than 0.4 mg. In protection tests, 2 mg. gave better results than 50 mg. of sulfanilamide. Its acute toxicity was, however, from 10 to 20 times that of sulfanilamide. In human beings, Buttle et al. found that after a single dose of 300 mg., the blood had definite antibacterial properties, but no detailed studies were reported. Subsequently, Buttle made a therapeutic trial in human beings with acute infections, using doses of the order of from 1 to 2 Gm. per day, but because of the rapid production of methemoglobinemia and other toxic effects, the treatment was soon abandoned.

The author, John Lowe, Director, Leprosy Research Unit, Nigerian Leprosy Service, Uzuakoli, Nigeria, has recently carried out further studies on DADPS from which he has made certain new conclusions.

In vitro and in animals the antibacterial power of DADPS is possibly the greatest of any of the sulfones. The accepted idea that DADPS is too toxic for

use in human beings was found to be erroneous. A regimen of oral administration of small doses, rising very slowly from 100 mg. per day to the standard 300 mg. a day in 5 weeks, is recommended, treatment being continuous. This regimen does not produce toxic effects of any consequence, and it will maintain a blood level of about 1 mg. per 100 ml., which on theoretical grounds was believed should be a therapeutic level in leprosy. The almost complete absorption from the gut and slow elimination by the kidney explain the relatively high blood level attained with such small doses, and also explains the toxic effects reported with the much higher doses used by others. In the avoidance of toxic effects, very slow induction of DADPS treatment is of paramount importance.

The author describes a trial of DADPS therapy in 88 patients with leprosy, for periods up to a year. Of the 50 patients with the lepromatous type of leprosy treated for more than 6 months, none showed deterioration; 72 percent showed clinical improvement; 62 percent showed bacteriological improvement; and 3 have become bacteriologically negative. These results compare very favorably with those seen using the complex proprietary sulfones (promin, diasone, and sulphetrone). There are indications that DADPS is acting more rapidly than these other sulfones. In 15 patients with the tuberculoid type of leprosy treated for from 4 to 10 months, the response has been apparent within a month, and sometimes within 2 weeks or less, with complete subsidence of activity of the skin lesions within 6 months; the nerve involvement, however, takes longer to subside. The results, though similar to, appear to be more rapid than, those seen with other sulfones in similar cases.

It is suggested that the more complex sulfones (promin, diasone, and sulphetrone) act by being hydrolysed to DADPS in the body. They are incompletely absorbed from the gut and incompletely hydrolysed to DADPS; they thus provide an unnecessarily elaborate and expensive method of securing the action of DADPS in the body.

The use of DADPS has certainly overcome the difficulty of the cost of sulfone treatment. Whether its use will reduce the duration of treatment remains to be seen. It has at any rate because of being cheaper in cost made sulfone treatment possible for a vast number of patients in tropical countries, whereas previous forms of sulfone treatment could not be more than the privilege of a few. The cost of DADPS for the treatment of one patient for a year on the basis of the dosage used is 14 shillings. The cost of the treatment with the complex proprietary sulfones is about 20 times as much. In Nigeria, treatment with hydnocarpus oil is now no cheaper than DADPS and in addition to the oil there is the big expense in syringes, needles, sterilization, and staff to give the injections. Moreover, the results are greatly inferior.

The present treatment regimen is based on a standard dose of 300 mg. given once a day. The question arises whether daily doses are necessary. A

small group of patients is being treated with twice-weekly doses given by mouth, the regimen being: first week, 100 mg. doses; second week, 200 mg. doses; and so on to 500 mg. doses in the fifth week, this dose then being maintained. The blood levels range from 2 mg. per 100 ml. soon after the dose to 0.3 mg. just before the next dose. Toxic effects are not serious, and clinical improvement is beginning to appear. Such a regimen would be suitable for outpatients and would reduce the cost of treatment to 7 shillings per year.

A further question that arises is whether, on daily administration, a dose of 300 mg. a day is necessary or advisable. This will be investigated later. The author and co-workers already know that in cases of tuberculoid leprosy, daily doses of 100 mg. are therapeutically active, but in these patients bacilli are very few and natural resistance is high. It would therefore be wrong to argue that 100 mg. is sufficient in heavily infective lepromatous cases with no natural resistance. Nevertheless, there are indications that improvement is not proportional to the size of the dose. Their patients on 400 and 500 mg. a day are not so far showing an appreciably more rapid improvement than those on lower doses, but the period of treatment is too short for a sound judgement. The best standard dose may turn out to be less than the present standard dose of 300 mg. daily.

The change in outlook in leprosy produced by sulfone treatment is one of the most striking achievements of modern medicine. The full action of sulfone treatment in severe cases is very slow but amazingly certain. The physician can now feel absolute confidence that an active case of leprosy, no matter how severe, will respond to the sulfone treatment, that the disease will cease to progress from the time when the treatment is begun, and that the lesions already present will slowly subside and the infection gradually die out.

Reconsideration of the sulfone treatment in tuberculosis may be advisable in the light of the findings recorded. Preliminary observations show that DADPS treatment as outlined for leprosy is well tolerated by patients with tuberculosis of the lungs. (Lancet, 28 Jan. '50)

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Observations on the Physiologic Effects of Cortisone and ACTH in Man: Until recently inadequate supplies of the adrenal cortex hormone, 17-hydroxy-11-dehydrocorticosterone, formerly known as compound E and hereinafter called cortisone, and pituitary adrenocorticotropic hormone, hereinafter called ACTH, have limited studies of the effects of these substances in man when administered in amounts sufficient to have pronounced physiologic activity.

With the development and improvement of methods for partial synthesis of cortisone and for the separation of larger amounts of ACTH from the pituitary

glands of animals, adequate amounts of both materials became available for trial in certain diseases of human beings.

The purpose of this paper is to present a brief review of the effects of these hormones on animals and human beings prior to the present era of their clinical application and to present a review of observations of their physiologic effects in human beings since September 1948. Special attention will not be given to questions of practical therapeutics. However, it is realized that such questions are implicit in any discussion of these hormones. The authors have had far more extensive experience with cortisone than with ACTH; therefore, cortisone will receive the greater attention. There is, however, no definite line of demarcation between the physiologic effects of these 2 agents. The results obtained through the use of cortisone apply in most respects to those with ACTH with the single exception of dosage: a quantitative measure of the amount of secretion delivered by the adrenal cortex after stimulation by ACTH is not possible.

Based upon the clinical and metabolic studies presented, as well as upon the observations of others on animals and human beings, the authors consider that ACTH and cortisone are powerful hormonal substances which are capable of influencing many physiologic processes. Their brief comment on some of the most conspicuous physiologic alterations observed follow.

Features of Cushing's Syndrome. Many of the manifestations of Cushing's syndrome were induced by protracted administration of cortisone. These included some features (mild hirsutism, acne, keratosis pilaris, mental depression, amenorrhea, edema, and alkalosis) which formerly were not thought by many (including some of the authors) to be caused by excessive amounts of cortisone-like steroids. In addition, certain other features of the syndrome which have been presumed in the past to be related to overproduction of cortisone-like steroids were observed. These included cutaneous striae, muscular weakness, impairment of carbohydrate tolerance, negative nitrogen balance and increased urinary excretion of corticosteroids. On the grounds that most of the classic features of Cushing's syndrome were observed within the group of patients who received relatively large amounts of cortisone, one can reasonably speculate that the entire syndrome as seen in association with hyperfunctioning lesions of the adrenal cortices may be the result of overproduction of cortisone-like steroid hormones. Final proof of this proposition is, of course, still lacking.

Urinary Steroids. If proof of the foregoing speculation concerning the pathogenesis of spontaneous Cushing's syndrome is forthcoming in the future, there is already good reason to suspect that 17-hydroxy-corticosterone (compound F) rather than cortisone may be the hormone responsible for the production of the syndrome. The principal lines of evidence in support of this supposition are: (1) the known similarity in the physiologic effects of compound F

and cortisone; (2) the isolation of relatively large amounts of compound F from the urine in certain patients undergoing study when the adrenal cortices were stimulated with ACTH, and (3) a similar finding in the case of a boy with spontaneous Cushing's syndrome associated with hyperplasia of the adrenal cortices. In any event, the evidence is suggestive that stimulation of the adrenal cortex of human beings by ACTH provokes the secretion of compound F rather than cortisone.

Excretion of corticosteroids was usually augmented during administration of cortisone. The same observation was previously made in the case of 2 female patients having Addison's disease who received cortisone. In both cases a small amount of unchanged cortisone was isolated from the urine. The amount of corticosteroids measured in the urine by chemical means was small relative to the amount of cortisone administered. Not more than 5 percent, and often much less of the cortisone administered could be found in the corticosteroid fraction.

The urinary excretion of 17-ketosteroids, on the other hand, decreased promptly when administration of cortisone was begun. In some cases the decrease persisted long after administration of the hormone was stopped. This evidence points to depression of at least some functions of the adrenal cortices by cortisone. The latter presumption is not invalidated by the observations that administered cortisone caused an increase in urinary excretion of 17-ketosteroids in female patients having Addison's disease and that large doses of cortisone in time caused an increase, rather than a decrease, in the 17-ketosteroids in the urine of patients in this series, all of whom presumably had intact adrenal glands. All these observations are consistent with the hypothesis, therefore, that 17-ketosteroids which appear in the urine during administration of cortisone are derived largely from administered cortisone. If this is true, the 17-ketosteroids excreted in these cases represented a maximum of only from 5 to 10 percent of the cortisone administered. After a long period of administration of the hormone, the amount which appeared in the urine as 17-ketosteroids was even less (only from 2 to 3 percent of the amount given).

Nitrogen. The loss of nitrogen which was observed during or after administration of large doses of cortisone (200 mg. daily) and ACTH (100 mg. daily) is indicative of an increase in the catabolism of protein under the influence of the hormones. Likewise, the retention of nitrogen which was observed when the effects of the administered hormones had waned is indicative of an antecedent loss of protein. The marked creatinuria which was observed when the hormones were administered probably has a similar general significance, for creatinuria commonly occurs in association with the metabolism of muscular tissue. The increased excretion of uric acid, sometimes unassociated with significant change in the level of uric acid in the blood serum, is probably consistent with the same interpretation.

Electrolyte Effects. As pointed out earlier, the details of the effects of cortisone and ACTH on electrolyte metabolism need further investigation. From a practical standpoint, however, it is apparent that these hormones may cause significant retention of salt and water, sometimes with the production of edema. That this effect may not persist, however, is indicated by the development of negative balances for sodium and chloride during continued administration of cortisone and the observation that edema may decrease or disappear in some patients while the hormone is being given.

Loss of potassium from the body under the influence of cortisone and ACTH is well documented. The experimental data indicate that in some instances a sufficient amount of potassium appears in the urine during administration of the hormones to indicate that it may be derived from both the extracellular and the intracellular fluid.

Carbohydrate Metabolism. Changes in carbohydrate tolerance as measured by determinations of the fasting blood sugar and by glucose tolerance tests were not pronounced. There is little reason to doubt, however, on the basis of Ingle's observations in rats, that the employment of larger doses of cortisone and ACTH or the presence of antecedent mild impairment of islet function would give rise to more conspicuous changes. In this connection, it should be pointed out that glycosuria observed during administration of cortisone or ACTH is not necessarily solely diabetic in character, for in the case of ACTH, at least, there is evidence which indicates that it depresses the renal threshold for glucose.

Functional Depression of the Adrenal Cortices. The evidence cited in the main body of this report is strongly suggestive of depression of some functions of the adrenal cortices by cortisone. The evidence consists of asthenia after withdrawal of cortisone, depression of the urinary excretion of 17-ketosteroids during administration and after withdrawal of cortisone and impairment of the eosinophilic response to ACTH. It seems probable that more conclusive evidence of depression of the adrenal cortices might become apparent if even larger doses of cortisone than were employed in this study were administered for prolonged periods. From a practical standpoint, the possibility should be borne in mind that function of the adrenal cortex might be inadequate under conditions of stress, such as fever or trauma, in a patient who had recently received cortisone.

Certainly the data which have been presented do not constitute an exhaustive investigation of the physiologic potentialities of these materials. Nevertheless, their far-reaching effects when given in sufficient dosage have been demonstrated. Although it is not the primary purpose to comment on questions of therapeutics, the inference of these observations is obvious; the profound physiologic effects of cortisone and ACTH will necessarily call for careful

consideration and a balance in their therapeutic use between what is most desirable from the standpoint of the disease in question, on the one hand, and what is best from the standpoint of the over-all welfare of the patient, on the other. (Arch. Int. Med., Feb. '50, R. G. Sprague et al.)

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Effect of Desoxycorticosterone Acetate (DOCA) and Ascorbic Acid on Formaldehyde-Induced Arthritis in Normal and Adrenalectomized Rats: The observation of Lewin and Wassen that a 5 mg. intramuscular dose of desoxycorticosterone acetate (DOCA), followed by from 0.5 to 1.0 Gm. of ascorbic acid intravenously relieves the symptoms of chronic polyarthritis is of great significance. The practical value of this treatment has been widely confirmed but in the fields of biochemistry and endocrinology, the observation may have even more far-reaching effects.

The stimulus for this work derived from the demonstration by Hench et al. that 100 mg. doses of a chemically defined sterol, cortisone, produced dramatically beneficial effects in chronic rheumatoid arthritis. In this connection it is of great importance that purified adrenocorticotropic hormone (ACTH) is also effective in rheumatoid arthritis. It is known that one effect of ACTH is to reduce the amount of ascorbic acid in the adrenal cortex, and indeed the method has been used for the quantitative estimation of ACTH (Sayers et al., 1948).

Two important points which have been observed in human beings are the disproportion between the dose of DOCA (5 mg. or less) and the dose of cortisone (100 mg.) and the fact that the ascorbic acid must be given parenterally. This discrepancy between the dose of DOCA and of cortisone may also be true in the rat. Selye used 5 mg. of cortisone in adrenalectomized animals to obtain protection similar to that seen with 1 mg. of DOCA plus ascorbic acid in the present experiments in adrenalectomized animals. It seems probable that a dose of 1 mg. of DOCA with ascorbic acid is unnecessarily large, particularly in the normal animal, but in the adrenalectomized animal such a dose is essential for complete survival. Under experimental conditions, the author and co-workers have established a quantitative titration curve for survival of adrenalectomized rats in the range of from 0.25 to 2.5 mg. of DOCA per 100 Gm. of rat. In this range, doses of from 2.0 to 2.5 mg. show chronic toxic effects. A dose of 1 mg. on the other hand gives almost complete protection against the effects of adrenalectomy for many weeks without toxic effects.

The points which have emerged from this work may be stated as follows:

1. The therapeutic effect of cortisone on chronic rheumatoid arthritis in human beings and its protective action against formaldehyde-induced arthritis in normal and adrenalectomized rats seem to have been reproduced by a combination of DOCA and ascorbic acid, both in man and in rats. Further, 5 mg. of DOCA with ascorbic acid appears to have approximately the same effect as 100 mg. of cortisone alone.

2. Ascorbic acid gives some protection against formaldehyde-induced arthritis in normal rats but not in adrenalectomized rats.

3. DOCA alone aggravates the experimental arthritis in normal rats but not (or only very slightly) in adrenalectomized rats.

DOCA plus ascorbic acid in the absence of endogenous adrenal hormones seems to be an effective substitute for the naturally occurring anti-arthritic sterol hormone. Because neither DOCA or ascorbic acid alone is effective in the adrenalectomized animal, both substances must be essential to the biochemical changes involved. The possibilities are either that both DOCA and ascorbic acid, perhaps with other substances in addition, are components of an essential enzyme system, or that DOCA must first be changed chemically (reduced) by ascorbic acid before it is effective.

The facts that ascorbic acid is present in the normal adrenal cortex but appears to be released therefrom by the administration of ACTH and that it gives some protection against formaldehyde-induced arthritis when given parenterally to the normal animal, strongly suggest that ascorbic acid takes part in the biochemical reaction in which the natural anti-arthritic sterol is involved. The fact that ascorbic acid given by mouth, although well absorbed, is ineffective indicates that the redox system may be implicated.

The aggravating effect of DOCA on inflammation is an intriguing observation. Does this mean that unaltered DOCA, although unsuitable as an anti-arthritic sterol, may nevertheless compete with the natural sterol hormone as a building unit and thus cause competitive inhibition, in the same way that sulfanilamide is thought to compete with p-aminobenzoic acid ? The apparent discrepancy between the positive effects seen in human beings with 5 mg. doses of DOCA combined with ascorbic acid, and the negative effects reported with 10 mg. doses of DOCA in combined therapy (Spies et al., 1949) may be explained by the aggravating effect of excess DOCA. (Lancet, 28 Jan. '50, G. Brownlee)

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Clinical Observations with Desoxycorticosterone Acetate (DOCA) and Ascorbic Acid: Since Lewin and Wassen reported their results with combined

injections of desoxycorticosterone acetate (DOCA) and ascorbic acid in rheumatoid arthritis - results the authors were able to confirm - the authors have made observations in 80 cases of rheumatoid polyarthritis and also in monarticular varieties of the disease in ankylosing spondylitis, and in osteoarthritis. In another field they have noted the action of these substances on painful stiff joints following injury, and on localized post-traumatic edema.

This report is chiefly concerned with the relatively transient clinical phenomena developing soon after single combined injections. Because it records the evolution and decline of this response, some importance may attach to the fact that all the injections on which it is based were given by one or the other of the authors and that in many cases progress was watched continuously for several hours afterwards.

The technic originally employed was that initially described by Lewin and Wassen in which 5 mg. of DOCA in peanut oil is given intramuscularly followed within 5 minutes by 1 Gm. of ascorbic acid intravenously (technic A). Later a single-dose intravenous technic was used with an aqueous solution of 5 mg. of desoxycorticosterone glucoside mixed in the syringe with the ascorbic acid (technic B). More recently they have been trying the effect of a single intramuscular dose of the oily DOCA and the aqueous ascorbic acid mixed in and given with one syringe (technic C).

In rheumatoid arthritis it is rare for no response whatever to occur at some time or another. In some cases it is dramatic, and apparent to the most superficial observation; and such a response provides one of the most exciting experiences of clinical medicine. In others it is slight but still recognizably of the same pattern. It not only varies from patient to patient but in the same patient from time to time. There are cases in which the initial response is barely appreciable but a second injection a week later is a dramatic success. The converse may also be true. In most instances the response is well established within one hour. In a few cases, using technic A, there has been a delayed reaction, coming on only after several hours. With technic B, the response has usually been apparent within 15 minutes. Technic C is as effective as the other methods; but, perhaps surprisingly, the response has been seen as soon as 2 or 3 minutes after injection and in some cases, the joint nearest the injection has been the first to show improvement.

A distinction must be made between measurable increase in joint range and the improved social performances allowed by the relief of pain and spasm; a patient with no great objective changes in the joints concerned may yet become comfortable enough to take off his coat, brush his hair, and climb stairs for the first time in many months. Although patients are often delighted with their new capacities, they exhibit no true euphoria. In some cases there is generalized decrease of sweating with local warmth over the affected joints.

Swelling, whether a result of synovial effusion or peri-articular edema may visibly shrink. The duration of the response varies between a few hours and several days, and is rarely as long as a week; but the end point is far from being as sharp as the onset. Although regression is usual, so that the disappointed patient may feel that he is back where he started, some objective improvement is usually retained, particularly in the shoulders; and when the response to the first injection has been a particularly good one, this level of improvement is not far short of the best that is attained after subsequent injections. The results are better in the monarticular than in the polyarticular forms of the disease; and in the latter, the shoulders, cervical spine, and wrists seem to react more favorably than do other joints. The reaction is nonspecific insofar as patients with active cases of ankylosing spondylitis and gonococcal arthritis respond in the same way. Osteoarthritis, however, is not affected except in certain circumstances detailed below.

The authors wish to draw attention to some effects produced by DOCA and ascorbic acid in certain traumatic states as illustrated by the following examples:

1. A woman, 51 years old, had fractured the head of her right radius 9 weeks before and had a painful range of motion of from 70° to 150° at that elbow. Fifteen minutes after injection (technic C) in the thigh, there was a painless range of from 45° to 165° accompanied by intense local warmth at and around the site of injury.

2. A 58-year-old man had fractured his right external malleolus 5 weeks before. When the plaster was removed, ankle motion was fair, but inversion and eversion of the foot at the subastragaloid joint were almost impossible and the attempt was very painful. Fifteen minutes after injection using technic C in the thigh there was a good easy inversion-eversion range estimated at 75 percent of normal with only slight pain and marked local warmth.

3. A 12-year-old girl had suffered a minor displacement of her left, lower, radial epiplysis 2 weeks previously and the range of wrist movement was between 15° dorsiflexion and 20° palmar flexion with pain and apprehension and severe local tenderness. Fifteen minutes after injection (technic C in the thigh) she had a full painless range without tenderness.

4. A 55-year-old man had slipped while working on a roof 3 days previously. An enormous hydrarthrosis developed, obscuring the normal contour and there were only a few degrees of very painful motion. Thirty minutes after the injection (technic C in the thigh), most of the effusion had subsided and there was a range of from 45° to 120° with only moderate discomfort, After this, progress was rapid without further injection and complete recovery in 10 days.

5. A 13-year-old girl had suffered a severe contusion of the right forearm muscles and as a result wrist movement was limited to a painful 20° arc. Fifteen minutes after injection (technic C), she had a full painless range and much of the swelling and tenderness of the affected muscle bellies had subsided.

Similar observations have been made in acute sprains of the ankle and the internal lateral ligament of the knee, in stiff, painful wrists after Colles's fractures, in stiff, edematous fingers after injury and tendon suture, and in impacted fractures of the neck of the humerus and lower end of the radius. The only instances of improvement in cases of osteoarthritis have been when there was associated ligamentous strain and edema such as is often found at the inner side of the osteoarthritic knee joint. In general, the regression after the initial response is much less in traumatic cases than in rheumatoid arthritis and sometimes a single injection suffices to clear up the whole condition, particularly in persistent localized post-traumatic edema. There is a close resemblance produced on the same conditions by blocking the sympathetic supply to the affected limb - viz., the corresponding actions on local temperature, skin color, and sweating.

The authors believe that DOCA and ascorbic acid act peripherally and not through the agency of the suprarenal gland or other internal organs. Their reasons are (1) that the response is so rapid, (2) that the response is, if anything, more rapid with technic C than with either A or B, and (3) that with technic C the response may appear first in the joint nearest the site of injection. The findings resulting from clinical experiments indicate that the interaction between DOCA and ascorbic acid when confined to the peripheral tissues is capable of producing all the observed clinical effects in the joints. This was well shown in 2 cases in which ascorbic acid was carried with the arterial flow to a limb containing a DOCA depot and from which the venous and lymphatic return had been occluded. (Lancet, 4 Feb. '50, D. LeVay and G. E. Loxton)

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Renal Hemodynamics in Heart Disease: Disturbances of renal function have long been known to exist in the presence of congestive heart failure. In 1944 Warren and Stead suggested that cardiac edema was secondary to retention of salt and water by the kidneys. These authors attributed the disturbances in renal function to a decreased cardiac output rather than to engorgement and possive congestion secondary to increased venous pressure. They further postulated that the disturbance might be more directly related to decreased renal blood flow. Merrill in 1946 and more recently Mokotoff and associates have clearly demonstrated a marked decrease in renal plasma flow and rate of glomerular filtration in congestive heart failure. For the authors of the present report it became of further interest, however, to determine whether these changes could be correlated with various phases of heart disease.

Furthermore, no previous studies of tubular function, utilizing the maximal tubular excretory capacity for para-aminohippurate, have been reported in patients with organic heart disease. Thus it was decided to include a study of this function as a part of the investigations.

Renal studies utilizing the clearance and saturation methods, devised by Smith, Goldring, Chasis, and co-workers, were conducted on 26 male patients with nonhypertensive organic heart diseases. Hypertensive patients were excluded because it was felt that renal vascular changes might be present out of proportion to the degree of cardiac involvement. Similar renal studies were conducted on eight normal men who were clinically free of cardiovascular and renal diseases. The small control series was established primarily as a check on the methods employed by this laboratory, for, adequate normal values have been established on larger groups by other investigators. The effective renal plasma flow and the maximal tubular excretory capacity were measured by the use of sodium para-aminohippurate, and the glomerular filtration rate was measured by the clearance of mannitol. Merrill has shown that the clearance of para-aminohippurate is a valid measure of the renal plasma flow in patients with congestive heart failure.

Based upon the data obtained, the authors consider that the changes in the effective renal plasma flow constitute the most striking disturbance of the renal hemodynamics in patients with organic heart disease. Of considerable interest was the finding of a diminished renal plasma flow in patients with rheumatic valvular heart disease who had never experienced heart failure. This finding was associated with a normal rate of glomerular filtration and a normal value for the maximal tubular excretory capacity for para-aminohippurate. The decrease in the effective renal plasma flow may represent one of the earliest hemodynamic changes in compensated valvular heart disease and indicates a shunt of blood from the kidneys even before the classical symptoms of congestive failure occur. The marked reduction of the effective renal plasma flow in congestive heart failure has been demonstrated previously and has been confirmed by the authors' investigations. With clinical compensation the renal plasma flow increases from that noted during decompensation but remains markedly reduced from normal and significantly less than that noted before the onset of congestive failure.

A reduction of the effective renal plasma flow might conceivably be a result of: (1) decreased arterial pressure, (2) increased venous pressure, or (3) renal arteriolar vasoconstriction. The arterial pressure is probably of little importance in this regard and was not found to differ significantly among the groups of patients studied. The role of increased venous pressure in the pathogenesis of decreased effective renal plasma flow has been a matter of dispute in the recent literature. Merrill has stated that a reduction of venous pressure to normal with mercurial diuretics has no effect on the renal blood

flow and has thus concluded that increased venous pressure is not a factor responsible for the decreased renal blood flow in congestive failure. On the other hand, Bradley and Bradley have shown that by increasing the intra-abdominal pressure in normal subjects they were able to increase the mean renal venous pressure to 18.3 mm. Hg.,(and concomitantly noted a decrease in the effective renal plasma flow, rate of glomerular filtration, and maximal tubular excretory capacity. It was concluded, therefore, that on the basis of their average data, the increase of renal venous pressure was usually sufficient to account for the reduction of effective renal plasma flow. Although there exists a relationship between venous pressure and renal plasma flow in patients with organic heart disease, it is obvious that the reduction in renal plasma flow is not caused primarily by changes in the venous pressure. It is conceivable that in patients with congestive heart failure an increased pressure in the venular end of the capillary bed might be a minor factor responsible for the reduction in the effective renal plasma flow.

In all phases of heart disease studied there was a disproportionate reduction in the effective renal plasma flow and rate of glomerular filtration. Thus it has been shown that in patients with congestive heart failure the renal plasma flow may be from 20 to 30 percent of normal and the rate of glomerular filtration reduced to only from 66 to 75 percent of normal. The maintenance of the glomerular filtration rate at a relatively high level in the presence of the great reduction of the renal plasma flow suggests a high degree of efferent arteriolar spasm which increases the effective intraglomerular pressure. This is reflected in the markedly elevated filtration fraction, and thus in congestive heart failure there is a considerably greater percentage of the plasma filtered per minute than occurs in normal subjects. The increased filtration fraction suggests that renal efferent arteriolar vasoconstriction is a prominent feature of all phases of organic heart disease. The mechanism of this vasospasm is unknown.

The relationship of effective renal plasma flow to cardiac output in all of the phases of heart disease cannot be completely evaluated at this time; however, it is of importance to note that Stewart and colleagues have previously demonstrated a reduction in the cardiac index in patients with compensated rheumatic valvular heart disease without previous evidence of heart failure. Furthermore, Merrill has shown that there is a significant correlation between cardiac output and renal plasma flow during congestive heart failure. However, the reduction in the renal plasma flow is proportionately greater than the reduction in the cardiac output and suggests that a renal regulatory mechanism produces a significant shunt of blood from the kidneys. The pathways by which this mechanism is mediated are unknown.

It seems to have been generally conceded that tubular function is normal in congestive heart failure. This assumption has been based primarily on the

observation that the kidneys are able to concentrate the urine in heart failure. It is, therefore, of extreme interest to note that there is a marked reduction in the maximal tubular excretory capacity for para-aminohippurate in decompensated patients, whereas it is normal in patients who are clinically compensated. Although it has been considered that the Tm_{pah} is a measure of the quantity of tubular mass, it is obvious that this relationship does not apply in congestive heart failure. The Tm_{pah} is actually a measure of the excretory capacity of the tubules and in no way can it be construed to indicate an anatomic number of nephrons. The fact that the Tm_{pah} reverts to normal with clinical compensation further emphasizes the functional aspects of this phenomenon. The specific mechanism involved in the decrement of the maximal tubular excretory capacity during congestive heart failure is unknown. The mechanisms which might conceivably be invoked are as follows: (1) an anatomic reduction of the number of nephrons, (2) intermittent glomerular occlusion, (3) blockage of low pressure nephrons by elevated venous pressure, (4) a specific loss of the tubular capacity to excrete para-aminohippurate, and (5) efferent arteriolar spasm of a severe degree resulting in tubular ischemia. The first hypothesis is untenable inasmuch as it has been demonstrated that the maximal tubular excretory capacity returns to normal with the restoration of clinical compensation. Intermittent glomerular activity has been shown to be an unlikely occurrence in the normal human kidney and it is improbable that this mechanism occurs in congestive heart failure. Furthermore, there is no evidence to suggest that afferent arteriolar spasm is a prominent feature during heart failure. Bradley and Bradley have stated that the reduction of maximal tubular excretory capacity noted during increased intra-abdominal pressure is a result of the increased renal venous pressure and related increased intrapelvic pressure. These factors would result in blockage of urine flow from low pressure nephrons. These authors state that the inactive nephrons would not contribute to the clearance of mannitol but the blood could be cleared of para-aminohippurate by neighboring operative tubules. If the reduction of the Tm_{pah} to 55 percent of normal were due to blockage of urine from low pressure nephrons, then it must be assumed that 45 percent of the glomeruli are inactive. Because the mean filtration fraction in this group of patients was 40.5 percent, it is apparent that the filtration fraction in the active glomeruli would have to attain exceedingly high values, probably in the range of from 70 to 80 percent. As noted by Smith and his associates it is unlikely that such high values could be attained. The hypothesis that the decrement in the maximal tubular excretory capacity in congestive heart failure is caused by a specific inability of the tubules to excrete para-aminohippurate cannot be evaluated at this time. It is known that this function may be reduced early in essential hypertension even though the renal plasma flow and rate of glomerular filtration are normal. It is also known that other factors can influence the excretory function of the tubules. Hypophysectomy has been shown to decrease the maximal tubular excretory capacity and vitamin A and testosterone to increase this function.

The reduction in the maximal tubular excretory capacity in heart disease occurs in the patients with the highest filtration fraction, that is, in those patients with the most marked degree of efferent arteriolar spasm. The assumption that this vasoconstriction might be so intense in localized areas of the kidneys as to result in renal ischemia and an actual decrease in the functional capacity of the tubules seems to be logical. If this mechanism is assumed to occur, one would expect to show that true renal ischemia occurs in congestive heart failure. That this actually does occur has been shown by Merrill who reported an increase in the arteriovenous oxygen differences in patients with congestive heart failure. Therefore, it seems likely that this single mechanism, which correlates well with the other observed changes in renal hemodynamics in congestive heart failure, might also be primarily responsible for the reduction in maximal tubular excretory capacity.

Though this study touches only indirectly upon the problem of the pathogenesis of cardiac edema, some interesting deductions can be formulated relative to this problem. There are obviously only 2 fundamental mechanisms by which the urinary excretion of sodium is controlled, namely, the rate of glomerular filtration and the amount of tubular reabsorption of sodium. Merrill and Mokotoff and his associates postulate that sodium retention results primarily from a reduced rate of glomerular filtration. If this were true, one would expect to find a significant difference in the glomerular filtration rates of the edematous and nonedematous patients with chronic heart failure. Since the volume of the glomerular filtrate is significantly reduced in chronic congestive heart failure, it is apparent that the amount of sodium presented to the tubules is reduced also. Thus this mechanism certainly is involved in the retention of salt and water. However, because the disappearance of edema associated with clinical compensation is not correlated with a significant increase in the rate of glomerular filtration in the authors' patients, the operation of another mechanism for salt and water retention is suggested. In the authors' patients the rate of glomerular filtration is not significantly changed as edema disappears, but there is a significant increase in the renal plasma flow and a fall in the filtration fraction. In 1942 Seymour and his co-workers noted similar changes in the renal function of 6 patients recovering from congestive heart failure; the rate of glomerular filtration (inulin clearance) showed no significant change, but the renal blood flow (phenol red clearance) increased to a degree approximating the increase in cardiac output. This suggests that in addition to decreased sodium filtration in heart failure there also must be an increase in the percentage of sodium reabsorption by the tubules. That tubular dysfunction exists in congestive heart failure is shown by the reduction of T_{mpah}. However, because of the well-known dissociation of tubular reabsorption and excretion, the T_{mpah} cannot be used as a criterion of the tubular reabsorption of sodium. It is conceivable that the markedly elevated filtration fraction noted in congestive heart failure might so disturb osmotic relationships in the kidney that the tubular reabsorption of sodium is enhanced. This hypothesis cannot be evaluated without further investigation of the mechanisms by which sodium excretion and retention occur in both normal persons and patients with heart disease. (Feb. '50, B. I. Heller and W. E. Jacobson)

Relation Between Blood Lipids and Excretion of Choline in Diabetic Patients: The increase of blood lipid fractions, diabetic-hyperlipemia, is a well-known sign of the abnormal fat metabolism which takes place in a system affected with diabetes mellitus.

The blood lipids can be divided into 3 groups, composed of (1) neutral fat, (2) phospholipids, and (3) cholesterol. Recent studies seem to indicate that practically all phospholipids contain choline, that is to say, they are composed of sphingomyelin and, mainly, of lecithin. Choline is regarded as an important dietary factor, playing an essential role in fat metabolism. In this laboratory the excretion of choline in the urine of persons with diabetes was investigated, and an increased choline output was found in some instances. In continuing these investigations, the relationship between the amount of choline excreted in the urine and the diabetic lipemia has been studied.

Twelve patients with diabetes, 5 men and 7 women, ranging in age from 24 to 57 years, average 39, served as subjects for this investigation. A history was taken and a complete clinical examination made in order to eliminate subjects with other conditions which are also known to affect the level of blood lipids (infections, cancer, thyroid dysfunction, etc.). The patients were given a hospital diet corresponding to common Swedish food, without restrictions regarding the amount and the composition. The experiments were usually carried out during the last days of hospitalization, when the patients had attained, as far as possible, a metabolic equilibrium with administration of sufficient amounts of insulin. Over a period of 3 days the 24-hour urine output was collected and the choline content estimated. The third morning about 9 a. m., after a fasting period of from 10 to 12 hours, 20 cc. of blood was collected and the blood lipids in the plasma estimated (as an anticoagulant 2 drops of a one-percent solution of heparin sodium were used). The subjects had eaten nothing since the previous evening meal, had indulged in no exercise, and were not emotionally disturbed by the procedure. The women patients were always tested about 2 weeks after a menstrual period. In the literature dealing with concentrations of blood lipid fractions, there is much uncertainty concerning the normal range of blood fats in the postabsorptive state. For this reason control determinations of blood lipids in normal subjects after the same fasting period, and on the same diet, were carried out. Estimations of choline in these normal subjects were not carried out, as it has been shown that the daily urinary excretion in normal persons shows variations up to 5 mg.

The methods adopted for determination of the choline in the urine and of the lipid phosphorus and cholesterol in the blood plasma were well tested and the experimental errors negligible; the results obtained in normal subjects were in agreement with the findings of other authors.

Because of technical difficulties, the level of free choline in the blood was not determined. The amounts of free choline are very small, viz. only about

0.5 mg. per hundred cubic centimeters of plasma, and for double estimations, from 35 to 40 cc. of blood are required.

From the data obtained, it is shown that there is a relationship between the amount of choline excreted in the urine and the blood level of lipid fractions, mainly between choline and phospholipids, as an increased amount of excreted choline is always accompanied with an increased lipid phosphorus content in the blood, and vice versa.

No correlation was found to exist between the high lipid phosphorus content of the blood and the severity of diabetic symptoms. Perhaps insulin does not act directly on the choline metabolism or on that aspect of fat metabolism connected with the function of the choline. (Arch. Int. Med., Feb. '50, O. V. Sirek, Stockholm, Sweden)

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The Effect of Topical Applications of Fluorides on Dental Caries in Young Adults: Because it has not yet been demonstrated that topical applications of sodium fluoride reduce dental caries in adults, it has commonly been assumed that fluoride applications are effective only in children. This idea has been strengthened by the failure of experiments using a fluoride dentifrice, a fluoride mouthwash, and a single application of an acid fluoride solution to give caries reductions in young adults. Some theoretical considerations also might suggest that fluorides might react less actively with mature than with newly erupted teeth. However, until clinical tests demonstrate that a treatment program which is effective in children is ineffective in adults, the conclusion that topical fluoride treatments do not prevent caries in adults is not warranted. This paper reports the effects on adults of a test of the sort which has repeatedly produced caries reduction in children.

At intervals of approximately 3 months, single quadrants of the teeth of 139 students, aged from 18 to 40 years, were treated with solutions of 1.0 percent sodium fluoride and 0.06 percent lead fluoride. After approximately 14 months, the quadrants treated with sodium fluoride showed 44.5 percent less new D.M.F. surfaces, or 56.6 percent less new carious surfaces, than did the untreated control quadrants on the opposite sides of the mouths. The quadrants treated with lead fluoride showed 27.5 percent less new D.M.F. surfaces, or 38.5 percent less new carious surfaces, than their control quadrants. (J. Dent. Research, Feb. '50, E. Klinkenberg and B. G. Bibby)

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Omission from BuMed Circular Letter 50-15: The 24 February Medical News Letter erred in omitting the material below which should be inserted after the paragraph that ends at the top of page 29.

8. All Reports of Medical Survey wherein the following provisions are applicable shall be forwarded via BuMed to BuPers or MarCorps, as appropriate, for final action:

BUMED CIRCULAR LETTER 50-19 16 February 1950

From: Chief, Bureau of Medicine and Surgery
To: Commanding Officers, U. S. Naval Hospitals (Continental)

Subj: NAVMED-102 Revised; Request for Submission of Special Report

Ref: (a) Par 5118, MMD, 1945

Encl: (1) Revised NAVMED-102
(2) Instructions for submitting revised NAVMED-102

This letter directs that after 1 February 1950, neuropsychiatric statistics be submitted weekly until notification is received to resume monthly reporting.

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BUMED CIRCULAR LETTER 50-20 Joint Letter 20 February 1950

From: Chief, Bureau of Medicine and Surgery
Chief of Naval Personnel
Commandant of the Marine Corps
To: All Ships and Stations

Subj: Naval and Marine Corps Reserve Aviators, Inactive; Physical Examination of

1. For purposes of promotion and for fulfilling the requirements of quadrennial physical examinations, inactive Naval and Marine Corps Reserve aviators may be examined at the same place and by the same board of medical examiners or medical officer as any other line officer in the Naval or Marine Corps Reserve.

2. Existing directives require members of the Organized Reserve to pass a flight physical examination, report of which must be made to the Bureau of Medicine and Surgery, within twelve months of the time they actually control service aircraft. For Volunteer Reserves this interval is six months. The report of any medical officer serving in an active-duty status or in a training-duty status in a department under the direction, authority and control of the Secretary of Defense, who is qualified to conduct flight physical examinations, is acceptable to fulfill these requirements. Therefore, when the services of medical officers of the U. S. Navy or U. S. Naval Reserve are not available, authority is granted to obtain, wherever possible, the services of medical officers of the U. S. Army or U. S. Air Force for conducting such flight physical examinations.

--BuMed. C. A. Swanson --MarCorps. C. B. Cates
--BuPers. J. W. Roper

Approved: 13 February 1950, Dan A. Kimball, Acting Secretary of the Navy

BUMED CIRCULAR LETTER 50-21 27 February 1950

From: Chief, Bureau of Medicine and Surgery
To: All Ships and Stations (less reserve fleets)

Subj: First-Aid Kit, Life Boat, Stock Number 9-214-825; First-Aid Kit, Life Raft, Stock Number 9-217-100; Availability and Requisitioning of

1. Initial stock of subject items which are to replace First-Aid Kit, Life Boat, Stock Number 9-214-775, and First-Aid Kit, Life Raft, Stock Number 9-217-125, are available for issue. Ships and stations currently authorized to stock the above material shall requisition the replacement items on BuMed Materiel Requisition (NavMed Form 4) from the nearest Naval Medical Supply Depot.

2. When replacement material has been received, First-Aid Kit, Life Boat, Stock Number 9-214-775, and First-Aid Kit, Life Raft, Stock Number 9-217-125, shall be expended from the records and the contents disposed of as outlined following:

(a) Transfer all narcotic drugs, regardless of quantity or condition to the nearest Naval Medical Supply Depot, unless required for use. Narcotic drugs shall be transferred on S&A Form 127 at no value and shipment made under security conditions.

(b) Retain usable material for use. Take up material retained for use under appropriation stock numbers as a gain by inventory.

(c) Survey and destroy unusable material at no value. C. A. Swanson

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